Sensory feedback signal derivation from afferent neurons

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QUARTERLY PROGRESS REPORT #7

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I   # Summary of the Overall Project

In this study we are exploring the feasibility of extracting 1) cutaneous sensory information about fingertip contact and slip, and 2) proprioceptive sensory information about wrist or finger position. We use implanted nerve cuff electrodes to record peripheral nerve activity in animal models.

Our overall **objectives** for the 3-year duration of this contract are as follows:

1. Investigate, in cadaver material, implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded.

2. Select a suitable animal preparation in which human nerve dimensions and electrode placement sites can be modeled and tested, with eventual human prosthetic applications in mind.

3. Fabricate nerve cuff electrodes suitable for these purposes, and subcontract the fabrication of nerve cuff electrodes of an alternate design.

4. Investigate the extraction of information about contact and slip from chronically recorded nerve activity using these animal models and electrodes. Specifically,

    a. Devise recording, processing and detection methods to detect contact and slip from recorded neural activity in a restrained animal;

    b. Modify these methods as needed to function in an unrestrained animal and in the presence of functional electrical stimulation (FES);

    c. Record activity for at least 6 months and track changes in neural responses over this time.

5. Supply material for histopathological examination from cuffed nerves and contralateral controls, from chronically implanted animals.

6. Investigate the possibility of extracting information about muscle force and limb position from chronically recorded neural activity.

7. Cooperate with other investigators of the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II.   # Summary of our Progress up to the Seventh Quarter

In the first year of this three year project we completed an investigation of the anatomy and possible implantation sites in three human cadaver arms (objective 1). We selected the cat forelimb as a suitable animal preparation in which to chronically implant recording devices to obtain cutaneous and proprioceptive afferent nerve signals during voluntary movements (objective 2). We implanted a series of eight cats, instrumenting nerves and muscles in the left forelimb with recording devices. We implanted four tripolar recording cuffs in each cat, two on the Median and two on the Ulnar nerves, along with recording EMG electrodes buried in the muscle belly of a primary paw flexor, Palmaris Longus, a ground wire, and a thermistor to record limb core temperature. By implanting two cuffs on each nerve, we were able to periodically monitor, under anaesthesia, nerve compound action potential (CAP) properties such as amplitude and conduction time that indicate the viability of the nerve and recording cuff interface. We also monitored cuff impedances and EMG pickup by the distal recording cuffs during stimulation of the proximal nerves. We followed the CAPs for at least a six month implant period (objective 4c).

We recorded nerve and muscle activity in each of the implanted cats during walking on a treadmill and we processed these signals to extract event-related responses such as paw contact from the ENG activity (objectives 4a, b). We started to design a computer-controlled forelimb reaching task and the hardware required to extract information related to paw contact and slip, muscle force, and limb position from chronically recorded nerve activity (objectives 4a, 4b, and 6).

We developed a histopathological protocol to investigate the condition of the nerves and implanted devices during a final acute surgery in which the recording devices were removed and nerve samples were taken from the implanted and contralateral control limbs for in-house and possible external examination (objective 5).

During the course of Year One, we fabricated approximately 60 tripolar nerve cuffs using fabrication techniques developed in-house. We also evaluated several nerve cuff designs produced by our sub-contractor Dr. Jerry Loeb (objectives 3 and 7), but these were found to be unsuitable and Dr. Loeb determined that he would not be able to meet the objectives of the subcontract, thus ending his participation on this project.

In the fifth quarter we performed a final acute surgery of the Year One series of chronically implanted cats. The average normalized CAP data from 9 nerves followed for 180 days was stable in both amplitude and conduction time. A number of CAP recordings were ended prematurely due to cuff wire breakage. We performed a study of the distribution of cutaneous field innervation of the paw from the Ulnar and Median nerves in the cat. Nerve samples were taken from 5 cats for histological examination (objective 5). In preparation for the Year Two series of implants, we selected 4 candidate muscles in the cat forelimb to retrieve proprioceptive information during movement (objective 6).

In the sixth quarter we implanted four of the Year Two series of chronically implanted cats with nerve cuffs on two of the Median, Ulnar, or Radial nerves and EMG electrodes in four forelimb muscles. We are monitoring CAPs under anaesthesia over the six-month implant period to determine nerve-cuff integrity, and we are also recording voluntary activity in the awake cat during walking on a treadmill and during a reaching and grasping task. A histopathological study of nerve samples from the Year One series of implants was initiated.

III. Summary of Progress in the Seventh Quarter

In the seventh quarter we implanted the fifth and sixth Year Two cats with nerve cuffs on the Ulnar and Radial nerves and EMG electrodes in the candidate muscles described in earlier progress reports. We continued our recording protocol of periodically monitoring the CAP under anaesthesia to determine the status of the nerves and recording devices (objective 4c). We have recorded voluntary nerve and muscle activity during walking on a treadmill and during a reaching and grasping task with a 1-D passive joystick (objectives 4a, 4b). We have initiated collaborative projects in analyzing the walking data with automatic rule-generating algorithms (objective 7). We presented preliminary results at Neural Prostheses: Motor Systems IV in Ohio in July, and we have generated ideas for a possible model of closed-loop control of functional electrical stimulation (FES) using afferent feedback. Finally, we have continued developing our histopathological protocols for investigating nerve tissue samples from our chronically implanted cats.

ᴵV.   Details of Progress in the Seventh Quarter

A.   Year Two implants

During the seventh quarter we implanted the 5th and 6th cats in our Year Two series of eight chronically implanted cats. The implanted devices consisted of two cuffs on each of the Ulnar and Radial nerves, as well as recording EMG electrodes in the forelimb muscles Palmaris Longus (Pal L), Flexor Carpi Ulnaris (FCU), Extensor Carpi Ulnaris (ECU), and Abductor Pollicis Longus (APL). Figure 1 shows medial and lateral views of the cat forelimb complete with implanted cuffs on the Median, Ulnar, and Radial nerves. In our two most recent implants, the distal Radial cuff has been substituted with a tripolar patch electrode (10*30 mm) sewn to the underside of the skin. A conventional cuff electrode would require the surgical dissection of nerve branches from the subcutaneous connective tissue and would result in a relatively bulky device directly under the skin, potentially causing injury to the nerve.
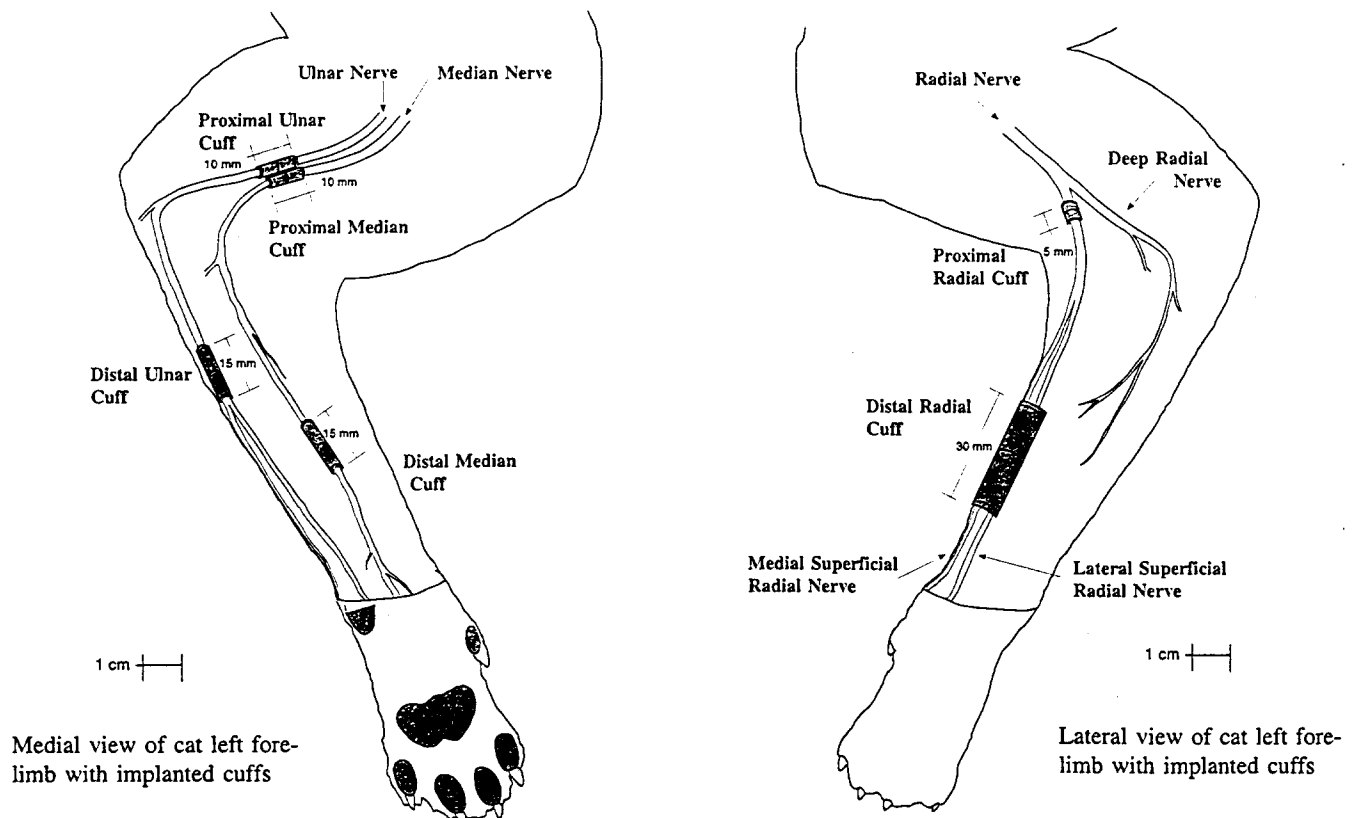

Medial view of cat left fore-
limb with implanted cuffs

Lateral view of cat left fore-
limb with implanted cuffs

Figure 1: Medial and lateral view of left cat forelimb with implanted cuffs on Median, Ulnar, and Radial nerves

B.   **Status of implants on Aug. 31, 1994**

To date we have implanted six Year Two cats and we have periodically monitored compound action potentials (CAPs) in order to evaluate the status of the nerve and recording devices. Table 1 summarizes the CAP data for each of the six implants in terms of number of days implanted and distal nerve CAP amplitude relative to day 0.

Table 1: Status of Year Two Implants as of Aug. 31, 1994

Subject	SX Date	Days implanted (as of Aug. 31)	Status of distal nerve CAP amplitude up to Aug. 31 (% of initial day 0 amplitude)
NIH 9	April 17, 1994	126	Ulnar - 80% Median - 19%, Prox cuff replaced on day 35
NIH 10	May 4, 1994	119	Ulnar - 140% Median - 90%
NIH 11	May 18, 1994	105	Ulnar - 70% Median - 121%
NIH 12	May 25, 1994	98	Radial - Prox wires broken on Aug. 18 87% prior to Aug. 18 Median - 125%
NIH 13	June 23, 1994	69	Ulnar - 87% Radial - 153%
NIH 14	June 30, 1994	62	Ulnar - 182% Radial - 149%

As of Aug. 31, we are recording CAPs from 92% (11/12) of the implanted nerves, compared to our success rate of 87% (13/15) at same time last year. Our single case of broken wires occurred in NIH 12, although there appears to be no nerve damage from pulled wires based on normal recordings from the distal Radial nerve cuff in the awake cat. In Year One, our primary source of problems was wires breaking due the cats scratching at local infections around the backpack sutures and wire exit points. In Year Two, we have implemented an improved silicone-clad backpack suture and we have not seen any evidence of the local infections described in Progress Report #4. In addition, we have added a belly band to restrict access to the backpack sutures and device wires.

The average CAP amplitude of the 10/12 nerves shown in Table 1 that have not suffered an obvious injury from initial compression or pulled wires is 120% ± 35% (1 SD), which suggests that the instrumented nerves are healthy and have not suffered any undue trauma. Note that we replaced the proximal Median cuff in NIH 9 on day 35 following a steep decline in CAP amplitude, and the amplitude has since recovered from < 1% to approximately 19% of the initial (day 0) amplitude.

C.   Walking Data Analysis

We have recorded nerve and muscle activity from the six chronically implanted cats walking on the treadmill at various speeds and inclines. The ENG and EMG signals are bandpass filtered to minimize noise, amplified to suitable levels, and stored on FM tape for off-line analysis. The off-line analysis consists of sampling (10 kHz for ENG and 1 kHz for EMG), and digitally rectifying and smoothing the signals to produce relatively clean waveforms for analysis. Figure 2 shows an example of data recorded from NIH 9 during walking on the treadmill at 0.5 m/s. The points of paw contact and lift-off were determined from frame-by-frame observations of video taken during the recording session.

Note the cyclic nature the distal nerve cuff signals, particularly the Ulnar, and also the cyclic nature of the two wrist flexors, Pal L and FCU. Of particular interest is the fact that both nerve signals appear to be in phase with the flexor activity and most active during stance. Note also the relatively small level of activity in the wrist extensors during locomotion. In our investigations, we have found differences in patterns of activity between cats and also changes in the same cat among successive steps.

In recording nerve activity during voluntary movements, it is important to minimize the EMG noise that contaminates and degrades the ENG signal. Figure 3 shows the distinct frequency spectra of the Ulnar nerve cuff and Palmaris Longus EMG signals for NIH 9 during walking, emphasizing minimal EMG contamination of the nerve cuff signal.

D.   Initiation of collaborative projects

We have initiated parallel collaborative projects with Dr. Dejan Popovic and Zoran Nicolic at the University of Miami, and with Dr. Dick Stein and Aleks Kostov at the University of Alberta. The purpose of these collaborative projects is to implement automatic rule-generating algorithms in the analysis of nerve and muscle data recorded in the cat forelimb during walking. To date, most FES systems implemented to restore locomotion or pinch grip are designed using stimulation patterns based on recorded EMG activity and personal experience. Our collaborations will investigate the use of automatic rule generators to analyze the nerve signals and predict muscle activity patterns, with the goal of developing intelligent systems and techniques that could be implemented in models of closed-loop control of FES with afferent neural activity used as feedback.
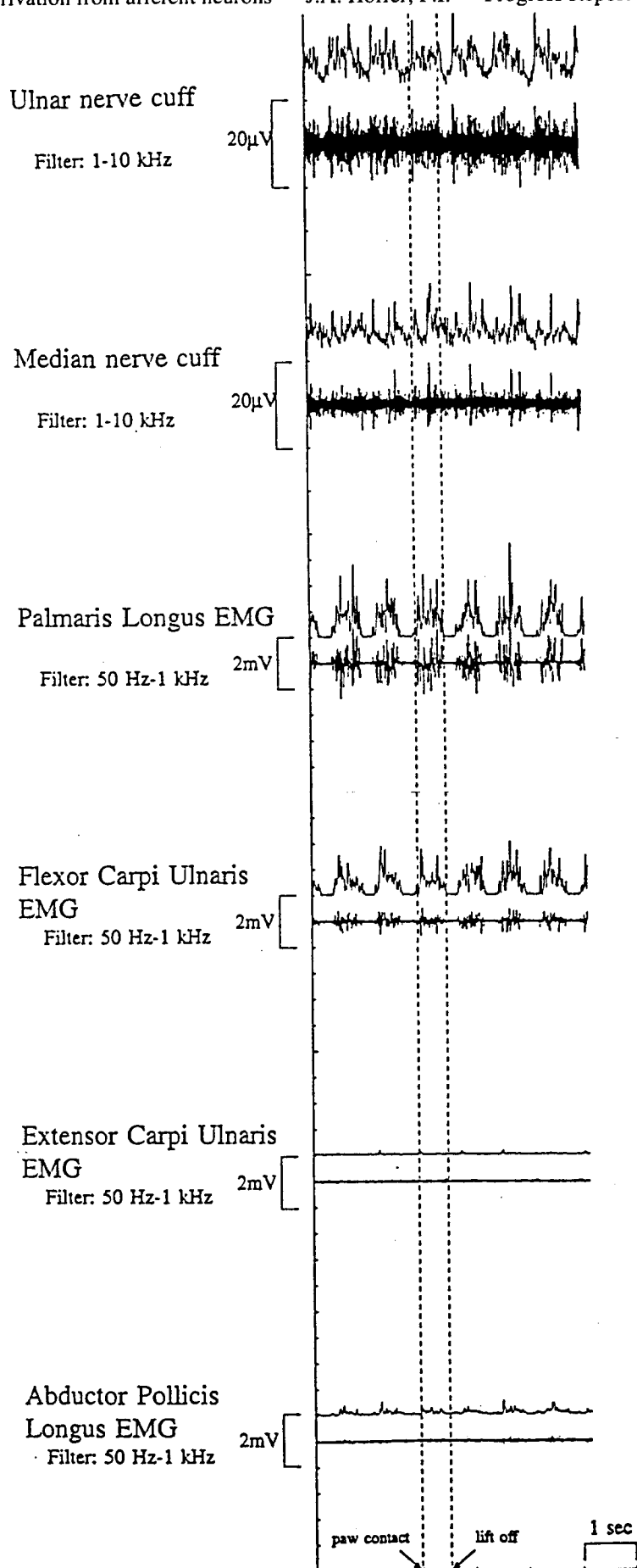
Ulnar nerve cuff

Filter: 1-10 kHz

20μV

Median nerve cuff

Filter: 1-10 kHz

20μV

Palmaris Longus EMG

Filter: 50 Hz-1 kHz   2mV

Flexor Carpi Ulnaris
EMG
Filter: 50 Hz-1 kHz   2mV

Extensor Carpi Ulnaris
EMG
Filter: 50 Hz-1 kHz   2mV

Abductor Pollicis
Longus EMG
Filter: 50 Hz-1 kHz   2mV

paw contact   lift off   1 sec

Figure 2: Nerve and muscle activity in NIH 9 during walking (0.5 m/s)

Ulnar nerve cuff

Palmaris Longus EMG
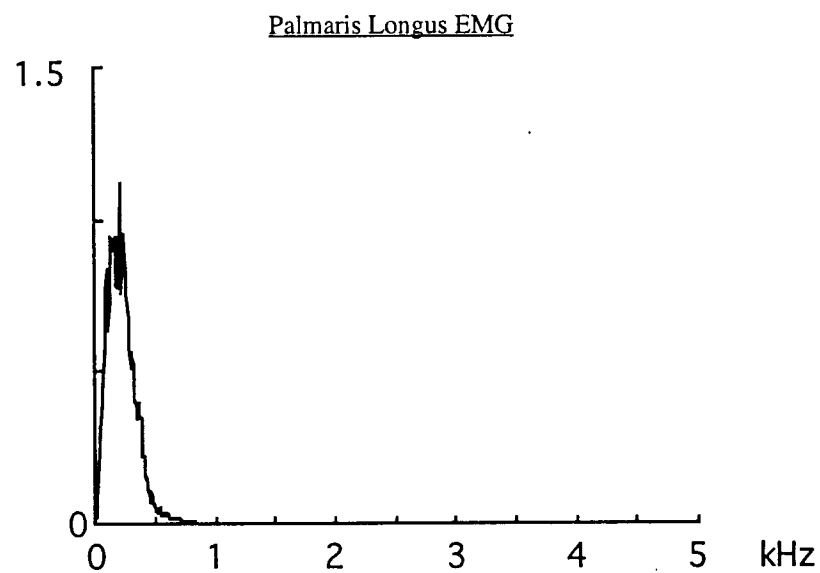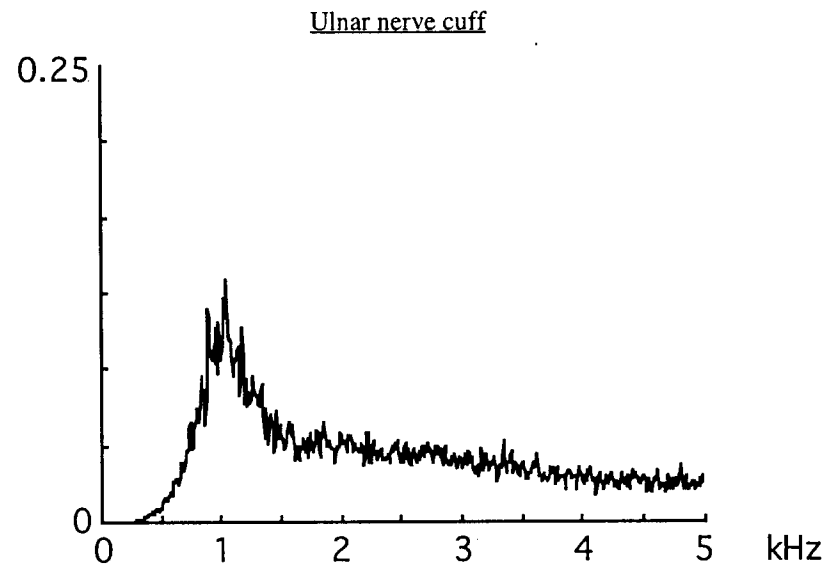
Figure 3: Frequency content of signals recorded in NIH 9 during walking

Ulnar nerve cuff

Filter: 1-10 kHz

20μV

Median nerve cuff

Filter: 1-10 kHz

20μV

Palmaris Longus EMG

Filter: 50 Hz-1 kHz

2mV

Flexor Carpi Ulnaris
EMG
Filter: 50 Hz-1 kHz

2mV

Extensor Carpi Ulnaris
EMG
Filter: 50 Hz-1 kHz

2mV

Abductor Pollicis
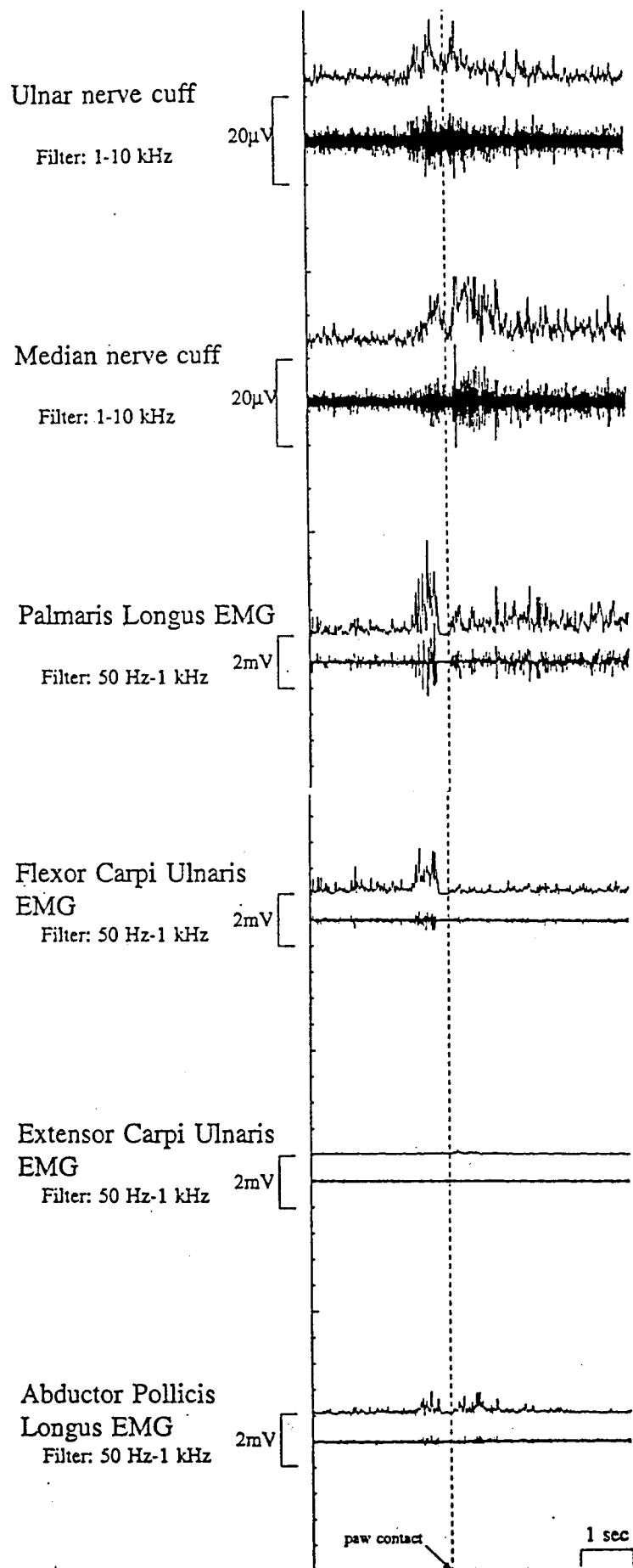Longus EMG
Filter: 50 Hz-1 kHz

2mV

paw contact

1 sec

Figure 4: Nerve and muscle activity in NIH 9 during a forelimb reaching and grasping task

E.   Reaching and Grasping Data Analysis

Figure 4 shows an example of nerve and muscle activity recorded from the cat forelimb during reaching and grasping a 1-D passive joystick. The cat is maintained in a comfortable sitting position by a jacket attached to a frame. He reaches with his forelimb, grasps the joystick with his paw, and pulls the joystick towards his mouth in order to retrieve a food reward. The dashed line marks the time of paw contact with the joystick.

Similar to the stance phase in the walking data, we see peaks of Ulnar and Median nerve activity following contact with the joystick during the grasping phase, as well as increased flexor activity during the grasping phase. The main difference between the walking data and the reaching and grasping recordings is the large amount of nerve and muscle activity prior to contact during the reaching phase unlike in the walking data where we see very little nerve or muscle activity during the swing phase. The nature of this activity prior to contact during reaching is still being analyzed.

Fig. 4 shows very little extensor muscle activity for subject NIH 9 during reaching and grasping which agrees with the walking data presented earlier for this particular cat, showing further similarities in muscle activation between tasks.

F.   Histolopathological examination of Year One cats

We have continued to develop the histopathological techniques that will be used to examine the nerve samples removed from the Year One implants. In the last quarter we investigated tissue sectioning and processing techniques as well as photomicroscopy and digital image processing procedures.

V. Plans for Eighth Quarter

In the eighth quarter we intend to:

1. continue histopathological examination of Year One cats (objective 5)

2. continue recording Year Two cats on treadmill and forelimb tasks (objective 4a)

3. design and construct cuffs appropriate for smaller proprioceptive nerves (objective 3)

4. complete the Year Two implant series

5. continue monitoring status of Year Two implanted nerves and electrodes (objective 4)

6. complete the construction of hardware for the reaching task (objective 4a,b)